MALIGNANT HYPERTHERMIA

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GLOSSARY OF TERMS

- ***HYPERMETABOLISM- ABNORMAL INCREASED USE OF MATERIAL BY THE BODY. INCREASED METABOLISM.***
- ***HYPERTHERMIA- ABNORMALLY HIGH BODY TEMPERATURE.***
- ***MH- AUTOSOMAL DOMINANTLY INHERITED CONDITION OCCURRING IN PT'S UNDERGOING GENERAL ANESTHESIA, ASSOCIATED WITH SIGNS OF INCREASED MUSCLE METABOLISM, SUCH AS TACHYCARDIA, TACHYPNEA, SWEATING, CYANOSIS, AND MUSCLE RIGIDITY.***
- ***HYPERCARBIA- EXCESS OF CARBON DIOXIDE IN THE BLOOD. (HYPERCAPNIA)***
- ***HYPERCAPNIA- RESIRATORY ACIDOSIS, RETENTION OF CO2.***

GLOSSARY OF TERMS

- ***ACIDOSIS- PATHOLOGIC CONDITION RESULTING FROM ACCUMULATION OF ACID OR DEPLETION OF THE ALKALINE RESERVE (BICARBONATE CONTENT) IN THE BLOOD AND BODY TISSUES AND CHARACTERIZED BY A DECREASE IN pH.***

- ***HYPERKALEMIA- ABNORMALLY HIGH POTASSIUM CONC IN THE BLOOD, OFTEN DUE TO DEFECTIVE RENAL EXCRETION.***

- ***HYPOXEMIA- DEFICIENT OXYGENATION OF THE BLOOD.***

- ***DEPOLARIZING AGENT- MUSCLE RELAXANT THAT PRODUCES SKELETAL MUSCLE PARALYSIS BY ALTERING THE ELECTRICAL STATE OF THE MUSCLE RECEPTOR, THUS BLOCKING MUSCLE RESPONSE TO NERVE IMPULSE.***

GLOSSARY OF TERMS

- ***ARRHYTHMIA- ANY VARIATION FROM THE NORMAL RHYTHM OF THE HEART.***
- ***VENTRICULAR TACHYCARDIA- ABNORMALLY RAPID VENTRICULAR RHYTHM WITH ABERRANT VENTRICULAR EXCITATION, USUALLY IN EXCESS OF 150 bpm.***
- ***TACHYPNEA- EXCESSIVE RAPIDITY OF RESPIRATION MARKED BY QUICK SHALLOW BREATHING.***
- ***CREATINE KINASE- AN ENZYME OF SKELETAL MUSCLE AND THE MYOCARDIUM, HELPS IN PRODUCING ATP.***
- ***MYOPLASMIC- RELATING TO THE CONTRACTILE PART OF THE MUSCLE CELL, OR MYOFIBRIL.***

GLOSSARY OF TERMS

- ***MYOGLOBIN- OXYGEN TRANSPORTING PIGMENT OF MUSCLE.***
- ***MYOGLOBINURIA- PRESENCE OF MYOGLOBIN IN URINE. MAY BE SEEN IN CRUSH INJURIES, AND AFTER PROLONGED EXERCISE IN SUSCEPTIBLE PERSONS (MUSCLE BREAKDOWN).***
- ***RHABDOMYOLYSIS- DESTRUCTION OF MUSCLE TISSUE ASSOCIATED WITH EXCRETION OF MYOGLOBIN IN URINE.***
- ***MYOPATHY- ANY DISEASE OF MUSCLE TISSUE.***
- ***SARCOPLASMIC RETICULUM- FOUND IN THE SARCOPLASM OF SKELETAL MUSCLE AND COMPRISING A SYSTEM OF SMOOTH SURFACED TUBULES FORMING A PLEXUS AROUND EACH MYOFIBRIL.***

GLOSSARY OF TERMS

- ***RECRUDESCENCE- RECURRENCE OF SYMPTOMS AFTER A PERIOD OF ABATEMENT. (AFTER DAYS VS RELAPSE- WEEKS)***

- ***TROPOMYOSIN- MUSCLE PROTEIN THAT INHIBITS CONTRACTION UNLESS ITS POSITION IS MODIFIED BY TROPONIN SO THAT THE MYOSIN MOLECULES CAN MAKE CONTACT WITH THE ACTIN MOLECULES.***

- ***TROPONIN- COMPLEX OF MUSCLE PROTEINS THAT INHIBIT CONTRACTION BY BLOCKING THE INTERACTION OF ACTIN AND MYOSIN; BUT WHEN COMBINED WITH Ca++, IT MODIFIES THE POSITION OF THE TROPOMYOSIN MOLECULES SO THAT INTERACTION TAKES PLACE.***

- ***CALCIUM- FOR PURPOSES HERE, AN ESSENTIAL DIETARY ELEMENT, A CONSTANT BLOOD Ca++ LEVEL ESSENTIAL FOR MAINTENANCE OF NORMAL HEARTBEAT, AND FOR NORMAL NERVE AND MUSCLE FUNCTION.***

GLOSSARY OF TERMS

- ***DISSEMINATED INTRAVASCULAR COAGULATION- CHARACTERIZED BY REDUCTION IN THE ELEMENTS INVOLVED IN BLOOD COAGULATION DUE TO THEIR UTILIZATION IN WIDESPREAD BLOOD CLOTTING WITHIN THE VESSELS.***

- ***DEATH- THE CESSATION OF LIFE; PERMANENT CESSATION OF ALL BODILY FUNCTIONS. CAN OCCUR IN THOSE WHO DEVELOP MALIGNANT HYPERTHERMIA.***

- ***MHAUS- THE MALIGNANT HYPERTHERMIA ASSOC OF THE UNITED STATES. DEDICATED TO THE CONTROL OF MH. MOST NOTABLE AND IMPT SERVICE IS MH HOTLINE; PROVIDES ACCESS TO PHYSICIANS WHO SPECIALIZE IN MH CRISES TX 24 HRS/D, 365 D/YR.***
- ***MH HOTLINE # 800-MH-HYPER***

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QUIZ

- ***TREATMENT OF MH INCLUDES***
- ***a) DANTROLENE***
- ***b) OXYGEN***
- ***c) VERAPAMIL***

- ***MALIGNANT HYPERTHERMIA***
- ***a) USUALLY INHERITED AS AUTOSOMAL RECESSIVE TRAIT***
- ***b) CAN BE CAUSED BY A DEFECT ON CHROMOSOME 19***
- ***c) MAY PRESENT WITH MASSETER MUSCLE SPASM***

QUIZ

- ***CHARACTERISTICS OF MALIGNANT HYPERTHERMIA INCLUDE:***

- ***A) AUTOSOMAL DOMINANT GENETIC TRANSMISSION.***
- ***B) IMPROVED SURVIVAL AFTER THE USE OF SODIUM DANTROLENE.***
- ***C) TRIGGERING BY LOCAL ANESTHETICS***

QUIZ

- ***TRUE / FALSE***

- ***DANTROLENE DECREASES Ca++ ION RELEASE FROM THE SARCOPLASMIC RETICULUM.***
- ***DANTROLENE MAY ALLEVIATE CHRONIC MUSCLE SPASTICITY.***
- ***MASSETER MUSCLE SPASM CAN BE AVOIDED BY NOT USING SUCCINYLCHOLINE.***

QUIZ

- ***TRUE / FALSE***
- ***ELEVATION OF END TIDAL CO2 IS A RELATIVELY SPECIFIC SIGN OF MALIGNANT HYPERTHERMIA.***
- ***HYPERTHERMIA 39-42°C IS A LATE SIGN IN MH.***
- ***NITROUS OXIDE CAN INDUCE MALIGNANT HYPERTHERMIA.***

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- ***BRIEF HISTORY***
- ***ETIOLOGY / PATHOGENESIS***
- ***CLINICAL PRESENTATION***
- ***INCIDENCE***
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- ***MANAGEMENT***
- ***A CONCERN IN DENTISTRY?***
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DEFINITION

- ***A LIFE THREATENING, ACUTE PHARMACO-GENETIC MYOPATHIC DISORDER DEVELOPING DURING OR AFTER GENERAL ANESTHESIA***

- ***TRIGGERED IN SUSCEPTIBLE INDIVIDUALS BY POTENT INHALATION ANESTHETICS AND DEPOLARIZING MUSCLE RELAXANTS***

- ***RESULTS IN HYPERMETABOLISM, SKELETAL MUSCLE DAMAGE, HYPERTHERMIA***

- ***DEATH RESULTS IF UNTREATED***

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MALIGNANT HYPERTHERMIA
BRIEF HISTORY:

- ***FIRST DESCRIBED BY DENBOROUGH AND LOVELL IN 1960 AND 1962 (ANESTHETIC DEATHS IN A FAMILY)***
- ***FIRST INTERNATIONAL SYMPOSIUM ON MH, TORONTO CANADA 1971***
- ***CAFFEINE-HALOTHANE CONTRACTURE TEST IDENTIFIED 1970/71***
- ***1970'S CONCLUSION: MH DUE TO METABOLIC CHANGES IN SKELETAL MUSCLE OF SUSCEPTIBLE INDIVIDUALS***
- ***1979 ANTIDOTE DRUG DANTROLENE IDENTIFIED FOR TX ACHIEVES FDA APPROVAL***

MALIGNANT HYPERTHERMIA
BRIEF HISTORY

- ***1980'S INVESTIGATIVE GROUPS FORMED IN UNITED STATES, CANADA, GREAT BRITAIN***
- ***1981 MALIGNANT HYPERTHERMIA ASSOCIATION OF THE UNITED STATES (MHAUS)***
- ***1987/88 NORTH AMERICAN MH REGISTRY***
- ***1995 MHAUS AND NORTH AMERICAN MH REGISTRY MERGE***
- ***1990'S INVESTIGATIONS CONTINUE TO IDENTIFY DEFECTIVE GENES IMPLICATED IN MH***

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ETIOLOGY / PATHOGENESIS

- ***HYPERMETABOLIC SYNDROME OCCURRING IN GENETICALLY SUSCEPTIBLE PATIENTS AFTER EXPOSURE TO VOLATILE ANESTHETIC TRIGGERING AGENTS. (SOME MH SUSCEPTIBLE FAMILIES HAVE DEFECT ON CHROMOSOME 19, RYANODINE RECEPTOR GENE).***

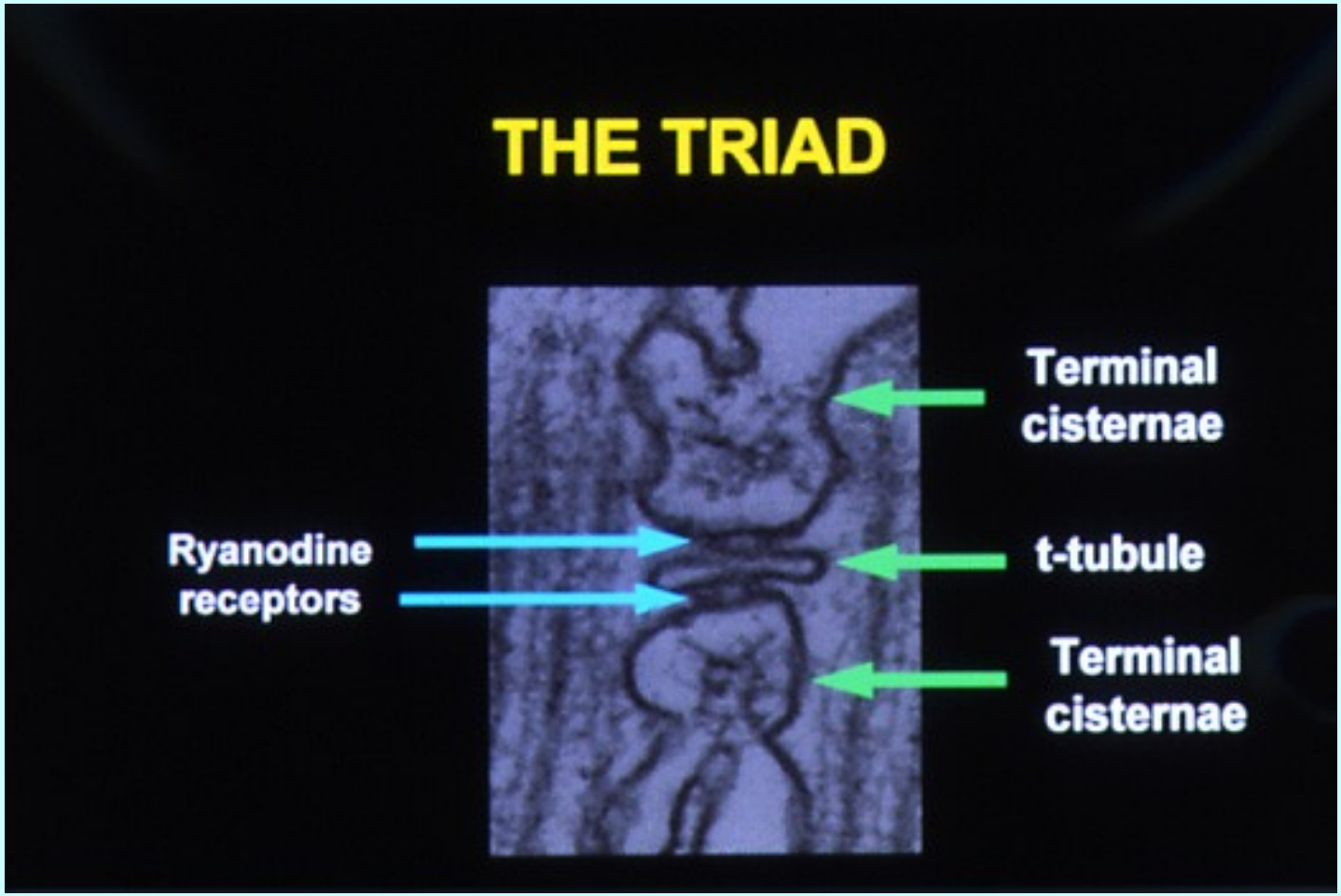
- ***TRIGGERING AGENTS INCLUDE HALOTHANE, ENFLURANE, ISOFLURANE, DESFLURANE, SEVOFLURANE, AND (DEPOLOR MUSCLE RELAX) SUCCINYLCHOLINE.***

- ***DEFECT CAUSES REDUCTION IN REUPTAKE OF Ca++ BY SARCOPLASMIC RETICULUM NEEDED FOR TERMINATION OF MUSCLE CONTRACTION.***

ETIOLOGY / PATHOGENESIS

- ***LEADS TO SUSTAINED MUSCLE CONTRACTION RESULTING IN SIGNS OF HYPERMETABOLISM, INCLUDING TACHYCARDIA, ACIDOSIS, HYPERCARBIA, HYPOXEMIA, AND HYPERTHERMIA.***
- ***FIRST SIGNS OF MH USUALLY OCCUR IN OPERATING RM BUT MAY BE DELAYED UNTIL PT REACHES RECOVERY RM.***
- ***INCREASE IN MYOPLASMIC CALCIUM PRESENT.***
- ***SKELETAL MUSCLE CONTRACTION DEPENDS ON RELEASE OF Ca++ FROM SARCOPLASMIC RETICULUM.***

ELECTRON MICROGRAPH OF THE JUNCTION OF THE SARCOPLASMIC RETICULUM AND THE T-TUBULES SHOWING THE SITE OF THE RYANODINE RECEPTOR (RyR-1).



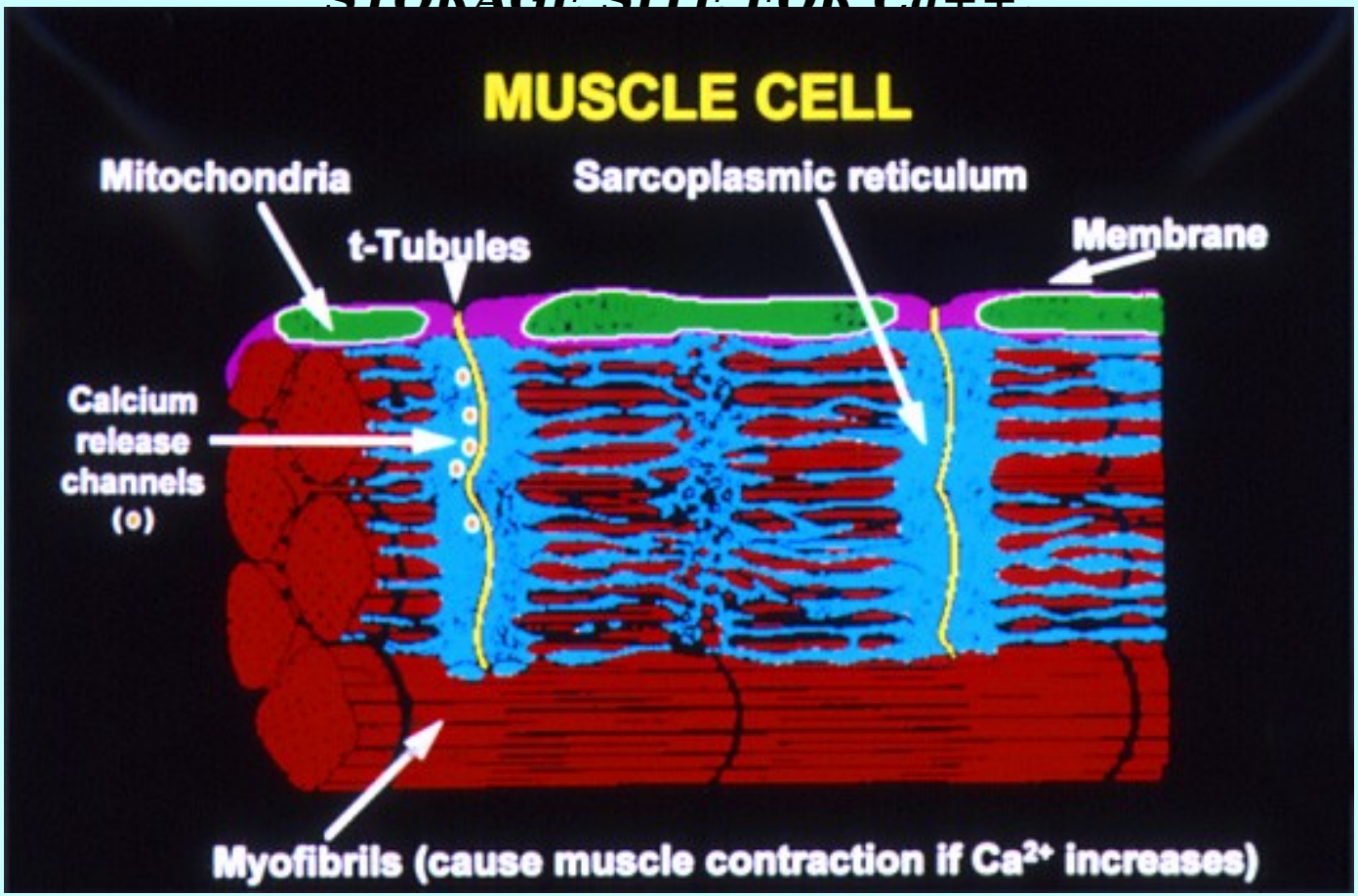
ETIOLOGY / PATHOGENESIS

- ***Ca++ RE-UPTAKE BY SACRCOPLASMIC RETIC IS NEEDED TO REVERSE THE PROCESS, IF DEFECT HERE THEN INCREASE MYOPLASMIC Ca++***
- ***INCREASED MYOPLASMIC Ca++ CAUSES PROLONGED CONTRACTION***
- ***CONTINUED ENERGY REQUIREMENTS LEAD TO INCREASED USE OF ATP, ACCUMULATION OF LACTIC ACID DUE TO ANAEROBIC METABOLISM***
- ***CULMINATES IN MUSCLE RIGIDITY, ELEVATED TEMPERATURE, METABOLIC ACIDOSIS***

ABNORMALITY IN MH.

THE CONTROLLED RISE AND FALL OF Ca++ LEVELS IN THE CELL LEADS TO MUSCLE CONTRACTION AND RELAXATION.

THE SARCOPLASMIC RETICULUM IS THE STORAGE SITE FOR Ca++



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MALIGNANT HYPERTHERMIA

CLINICAL PRESENTATION:

- ***UNEXPLAINED TACHYCARDIA***
- ***HYPERCARBIA***
- ***TACHYPNEA***
- ***ACIDOSIS (metabolic and respiratory)***
- ***MUSCLE RIGIDITY. MASSETER MUSCLE SPASM (MMS) AFTER GIVING SUCCINYLCHOLINE IS ASSOCIATED WITH MH. HOWEVER NOT ALL PT'S WHO DEVELOP MMS WILL DEVELOP MH. 30-50%***

CLINICAL PRESENTATIONS

- ***HYPOXEMIA***
- ***VENTRICULAR ARRYTHYMIAS***
- ***HYPERKALEMIA***
- ***INCREASE TEMPERATURE IS A LATE SIGN (39-42°C)***
- ***MYOGLOBINURIA***

CLINICAL PRESENTATION

- ***LATE SIGNS:***
  INCREASED TEMPERATURE 1-2°C EVERY 5 MINUTES

- ***RHABDOMYOLYSIS, MYOGLOBINURIA, DISSEMINATED INTRAVASCULAR COAGULATION***

- ***RISK OF RECRUDESCENCE AFTER STABILIZATION 24-36 HRS IS 25%***

- ***DEATH IF UNTREATED (10% EVEN IF TX PROPERLY)***

REVIEW CARDINAL SIGNS OF MALIGNANT HYPERTHERMIA

- ***SUSTAINED, SIGNIFICANT HYPERMETABOLISM***
- ***INHERITED COMPONENT - AUTOSOMAL DOMINANT***
- ***ABNORMAL SKELETAL MUSCLE BIOCHEMISTRY***

MALIGNANT HYPERTHERMIA

- **SPECIFIC SIGNS**
- ***MUSCLE RIGIDITY***
- ***INCREASED END TIDAL CO2 PRODUCTION*****
- ***RHABDOMYOLYSIS***
- ***MARKED TEMPERATURE INCREASE***

- **NON SPECIFIC SIGNS**
- ***TACHYCARDIA***
- ***TACHYPNEA***
- ***ACIDOSIS (RESPIRATORY AND METABOLIC)***
- ***HYPERKALEMIA***

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INCIDENCE OF MALIGNANT HYPERTHERMIA

- ***EXACT INCIDENCE UNKNOWN***
- ***MOST COMMON IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS***
- ***ALL RACES & ETHNIC BACKGROUND AFFECTED***
- ***OCCURRENCE RATE ESTIMATED BETWEEN ONE IN 5000 TO ONE IN 65,000 (3000-100,000 SOME STUDIES) ADMINISTRATIONS OF GEN ANESTH WITH TRIGGERING AGENTS.***
- ***INCIDENCE VARIES DEPENDENT UPON CONC OF MH SUSCEPTIBLE FAMILIES WITHIN GEO AREA.***
- ***HIGH INCIDENCE AREAS IN U.S.A. INCLUDE, WISCONSIN, WEST VIRGINIA, AND MICHIGAN.***

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DIAGNOSIS / TESTING

- ***MOLECULAR GENETIC SCREENING***
- ***NOT AN OPTION AT THIS TIME.***
- ***GENE CODING FOR Ca++ RELEASE IS ON CHROMOS 19.***
- ***- PRESENTLY 15 KNOWN MUTATIONS LINKED TO MH.***
- ***SIMPLE GENETIC SCREENING FOR MH NOT FOR YEARS.***

- ***CONTRACTURE TESTING***
- ***CAFFEINE-HALOTHANE-CONTRACTURE-TEST***
- ***- (CHCT)***

DIAGNOSIS / TESTING

- ***GOLD STANDARD AND CURRENT METHOD OF DIAGNOSING MH IS CONTRACTURE TESTING BY CAFFEINE-HALOTHANE-CONTRACTURE-TEST (CHCT) IN A MUSCLE BATH APPARATUS.***

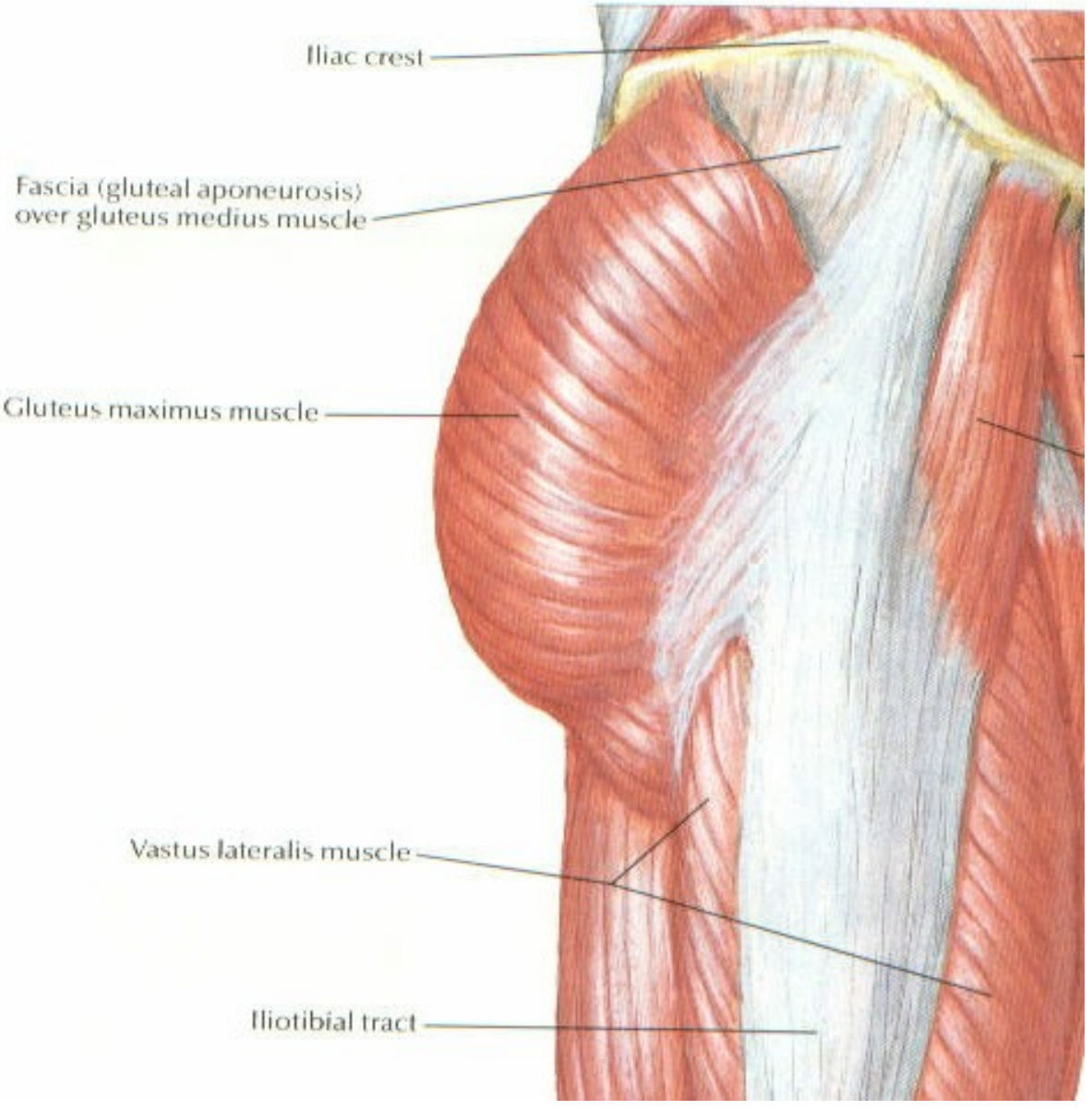
- ***EXPENSIVE (> $2500), INVASIVE, NON-ROUTINE PROCEDURE DONE AT SPECIFIC DIAGNOSTIC CENTERS (TWELVE IN U.S.A. AND CANADA).***

- ***FRESHLY BIOPSIED SKELETAL MUSCLE TISSUE.***

- ***MUSCLE OF CHOICE IS THE VASTUS LATERALIS.***

- ***2-3g MUSCLE NEEDED TO PERFORM TESTING.***

Muscles of Hip and Thigh: Lateral View



CAFFEINE HALOTHANE CONTRACTURE TEST
MUSCLE BATH APPARATUS

- ***RATE AND TENSION AT WHICH MUSCLE CONTRACTS AFTER EXPOSURE TO CAFFEINE AND HALOTHANE IS RECORDED ELECTRONICALLY.***

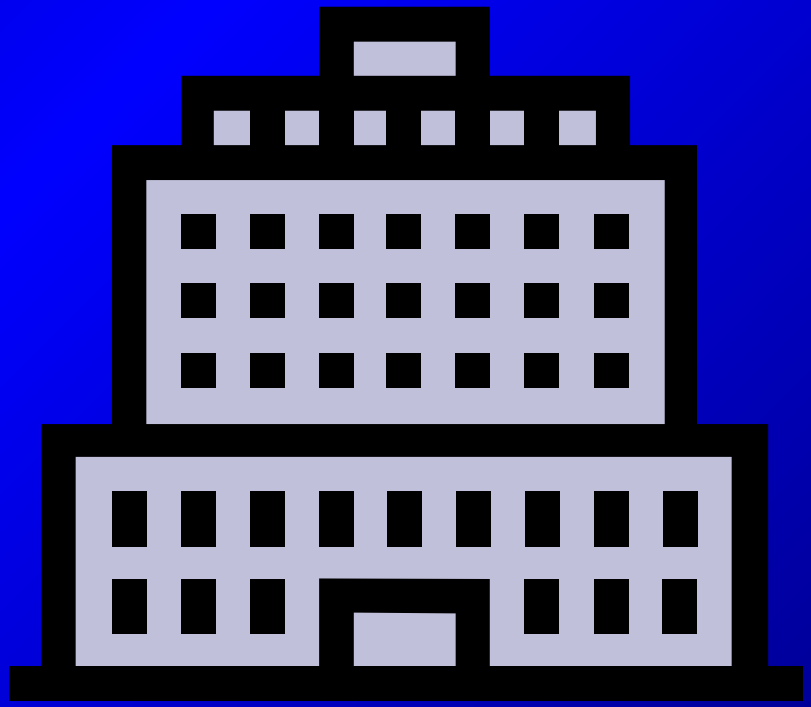
- ***MUSCLE FROM MH SUSCEPTIBLES MORE SENSITIVE & CONTRACTS WITH GREATER SUSTAINED FORCE.***

- ***COMPARISON OF STRENGTH OF CONTRACTION (MUSCLE TENSION) WITH PREVIOUS ESTABLISHED STANDARDS DETERMINES MH SUSCEPTIBILITY.***

MUSCLE BIOPSY CENTERS

- *U.S.A.*
- *BETHESDA, MD*
- *CHICAGO, IL*
- *LOS ANGELES, CA*
- *MINNEAPOLIS, MN*
- *PHILADELPHIA, PA*
- *ROCHESTER, NY*
- *SACRAMENTO, CA*
- *TAMPA, FL*
- *WINSTON SALEM, NC*

- *CANADA*
- *OTTOWA*
- *TORONTA*
- *WINNEPEG*



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IMMEDIATE THERAPY FOR MALIGNANT HYPERTHERMIA

HAVE A PLAN AND MOVE

MANAGEMENT OF MALIGNANT HYPERTHERMIA

- ***DISCONTINUE ANESTHESIA AND CURTAIL SURGERY IMMEDIATELY***
- ***HYPERVENTILATE PT WITH 100% OXYGEN***
- ***GET ADDITIONAL HELP***
- ***ADMINISTER DANTROLENE 2.5MG/KG IV BOLUS***
- ***COOL THE PT: COLD IV NORMAL SALINE, COLD BODY CAVITY LAVAGE, ICE BAGS, COOLING BLANKET***

MANAGEMENT OF MALIGNANT HYPERTHERMIA

- ***MONITOR AND TREAT ACIDOSIS: ADMINISTER SODIUM BICARBINATE***
- ***PROMOTE URINE OUTPUT- MANNITOL 25 gm IV, FUROSIMIDE 20 mg IV, &COPIOUS IV FLUID***
- ***TREAT ARRHYTHMIAS - DO NOT USE CALCIUM CHANNEL BLOCKERS***
- ***MONITOR URINE MYOGLOBIN***
- ***MONITOR COAGULATION STUDIES FOR 24-48 HRS***

DANTROLENE (DANTRIUM)

- ***ONLY KNOWN SPECIFIC TREATMENT FOR MH.***

- ***EFFICACY DUE TO ABILITY TO INHIBIT Ca++ RELEASE FROM SARCOPLASMIC RETICULUM***

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MH… A CONCERN IN DENTISTRY ?

- ***MH SHOULD BE ADDRESSED AS SERIOUS CONCERN IN OMFS AND OTHER DENTAL PRACTICES WHERE GENERAL ANESTHESIA IS USED.***

- ***ALL PT'S QUESTIONED ON UNTOWARD GENERAL ANESTHESIA EXPERIENCE (SELF & FAMILY HX)***

- ***ANESTHETIC CONSIDERATIONS - ALL CLASSES OF L.A. (AMIDES AND ESTERS) ARE SAFE WITH MH SUSCEPTIBLES.***

- ***NITROUS OXIDE IS CONSIDERED A SAFE AGENT.***

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SUMMARY

- ***MH IS A METABOLIC MYOPATHY THAT AFFECTS SKELETAL MUSCLE***
- ***ALL POTENT VOLATILE INHALATION ANESTHETICS AND SUCCINYLCHOLINE ARE THE TRIGGERS FOR MH***
- ***INHERITANCE OF MH IN HUMANS IS AUTOSOMAL DOMINANT***
- ***THE BASIC DEFECT IN MH IS AN INCREASE IN INTRACELLULAR CALCIUM OF THE SKELETAL MUSCLE***
- ***MH AFFECTS ALL AGES AND RACES***
- ***MH APPEARS TO BE MORE COMMON IN CHILDREN THAN ADULTS***

- ***MASSETER MUSCLE RIGIDITY AFTER SUCCINYLCHOLINE IS ASSOCIATED WITH MH IN 30-50% OF CASES***
- ***END TIDAL CO2 INCREASE IS THE MOST SENSITIVE AND SPECIFIC CLINICAL SIGN***
- ***HYPERTHERMIA IS A LATE SIGN OF MH BUT IS AN IMPORTANT CONFIRMATORY SIGN IN SOME CASES***
- ***METABOLIC AND RESPIRATORY ACIDOSIS ARE COMMON***
- ***MYOGLOBINURIA AND ELEVATED CK ARE COMMON DURING AND AFTER MH***

- ***MH MAY APPEAR AT ANY TIME DURING ANESTHESIA AND IN THE EARLY PART OF THE RECOVERY PERIOD***
- ***PROMPT TREATMENT WITH DANTROLENE 2.5MG/KG OR MORE EFFECTIVELY TREATS MH***
- ***DANTROLENE SHOULD BE CONTINUED FOR 24-48 HRS***
- ***THE ONLY ACCEPTED DIAGNOSTIC TEST IS THE CAFFEINE-HALOTHANE CONTRACTURE TEST***
- ***MH TESTING IS INDICATED IN PATIENTS WITH CLINICAL EPISODES AND THEIR FAMILY MEMBERS***

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CONCLUSION

- ***MODERN MONITORING, BETTER KNOWLEDGE OF MH BY THE ANESTHETISTS AND PROMPT THERAPY USING DANTROLENE REDUCES THE INCIDENCE OF THE CLASSIC MH CRISIS. NEVERTHELESS, MH IS STILL POTENTIALLY LIFE THREATENING, AND ANYONE WHO IS INVOLVED WITH ANESTHESIA, AND ANESTHETICS SHOULD HAVE UP TO DATE KNOWLEDGE ABOUT DIAGNOSIS AND THERAPY OF MH.***

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EXTRA CREDIT ?

- A SHIP IS LYING IN THE HARBOR. OVER ITS SIDE HANGS A ROPE LADDER WITH ITS END JUST TOUCHING THE WATER. THE RUNGS OF THE LADDER ARE ONE FOOT APART. THE TIDE RISES AT THE RATE OF EIGHT INCHES AN HOUR. AT THE END OF SIX HOURS HOW MANY RUNGS ARE COVERED?

MALIGNANT HYPERTHERMIA

- THE END

MALIGNANT HYPERTHERMIA

- QUESTIONS